DETAILED ACTION

Election Acknowledged

1. Applicants' election without traverse the invention of Group I encompassing claims 1-17 is acknowledged. The restriction is made final without traverse. Therefore, the restriction requirement is deemed to be proper and made final.

2. However, Applicant was subject to a species election but upon further consideration this requirement has been withdrawn.

3. Claims 1-20 are pending, claims 18-20 are withdrawn and claims 1-17 are presented for examination on the merits. The following rejections are made.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. **Claims 1-4, 6-9 and 11-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Wain et al. (WO00/45795; of record, see IDS), evidenced by STN search results.**

6. Wain et al. ('Wain) is drawn to a topical medicinal spray composition which comprises one or medicaments in a non-aqueous vehicle and one or more film forming polymers (see abstract). Example 12 discloses a sample spray formulation which comprises the pharmaceutically active agent estradiol at a concentration of 1 % w/w (see instant claims 1 and 15-17), the film forming polymers PVP-VA (i.e. polyvinylpyrrolidone-vinyl acetate copolymer,

VP/VA, see STN search results) at a concentration of 4 % w/w (see instant claims 1-4), the anti-nucleating agent PVP K-30 (polyvinylpyrrolidone, see STN search results) at a concentration of 6 % w/w (see instant claims 6-8) and the non-aqueous solvents acetone, methylene chloride and ethanol which are contained at concentrations of 27 %m 28 % and 28% w/w, respectively (see instant claims 1 and 13-14). The sum of the non-aqueous solvents results in a non-aqueous vehicle which comprises at least about 60 % by weight of the formulation (see instant claim 12). The composition of Example 12 also comprises polyethylene glycol 6000 and polyethylene glycol at a concentration of 2 % and 3 % w/w/, respectively for a total of 5%. It is taught in the specification of Wain that polyethylene glycols are polyhydric alcohols, which in turn are skin permeation enhancers (see page 7, 5th paragraph and page 8, 3rd paragraph; see instant claims 9 and 11).

7. Thus, the limitations of the instantly rejected claims are met entirely by Wain.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. **Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wain et al. (WO 00/45795; of record, see IDS) in view of Foldvari (PSTT, 2000, 3(12), 417-425).**

10. Wain et al. ('Wain) is drawn to a topical medicinal spray composition which comprises one or medicaments in a non-aqueous vehicle and one or more film forming polmers (see abstract). Example 12 discloses a sample spray formulation which comprises the pharmaceutically active agent estradiol at a concentration of 1 % w/w (see instant claims 1 and 15-17), the film forming polymers PVP-VA (i.e. polyvinylpyrrolidone-vinyl acetate copolymer, VP/VA, see STN search results) at a concentration of 4 % w/w (see instant claims 1-4) and the anti-nucleating agent PVP K-30 (polyvinylpyrrolidone, see STN search results) at a concentration of 6 % w/w (see instant claims 6-8). It is noted that Wain states that the film forming polymer can be contained in the composition from 0.1% to 10% w/w (see claim 5; see instant claim 5). The composition of Example 12 also contains the non-aqueous solvents acetone, methylene chloride and ethanol which are contained at concentrations of 27 %, 28 % and 28% w/w, respectively (see instant claims 1 and 13-14). The sum of the non-aqueous solvents results in a non-aqueous vehicle which comprises at least about 60 % by weight of the formulation (see instant claim 12). The composition of Example 12 further comprises polyethylene glycol (PEG) 6000 and polyethylene glycol at a concentration of 2 % and 3 % w/w, respectively for a total of 5 %. It is taught in the specification of Wain that polyethylene glycols are polyhydric alcohols, which in turn are skin permeation enhancers (see page 7, 5th paragraph and page 8, 3rd paragraph; see instant claims 9 and 11).

11. Wain fails to teach transdermal permeation enhancers as being selected from menthol, dimethylisosorbide, glycerylmonooleate and myristyl lactate.

12. Foldvari is a review article drawn to non-invasive administration of drugs through the skin. It is taught that menthol (terpene) is a useful penetration enhancer which acts by disrupting

intercellular lipid orders (see instant claim 10). Moreover, addition of menthol to skin increases net electrical conductivity which indicates the opening of polar pathways in the stratum corneum and allows for simplifying the passage of active agents (see Table 1, page 420).

13. Thus, one ordinarily skilled in the art, at the invention was made would be motivated to combine the teachings of Wain and Foldvari with a reasonable expectation for success in arriving at a transdermal spray formulation comprising a pharmaceutically active agent, a VP-VA copolymer, a non-aqueous vehicle, a penetration enhancer, and a anti-nucleating agent at the required weight percentages. Wain teaches a composition which comprises an active agent (estradiol), an anti-nucleating agent (PVP-k 30), a film forming polymer (PVP-VA), penetration enhancer (PEG) and non-aqueous solvents acetone (acetone, ethanol and methylene chloride). Although Wain includes penetration enhancers in their composition, Wain fails to specifically disclose using menthol as such. Foldvari et al. is a review article drawn to penetration enhancers and their use to improve transdermal delivery of pharmacologically active agents. It is specifically taught that menthol is useful as a penetration enhancer. As Wain motivates using a penetration enhancer in the composition, it follows that employing any penetration enhancer would be useful so long as it fulfills the role of performing its function. If one arrived at menthol out of the many potential enhancers and the product was successful, such a result would not be due to innovation but rather due to ordinary skill and common sense. Therefore, the invention as a whole is *prima facie* obvious to one ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

15. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
April 1, 2008

/Michael P Woodward/
Supervisory Patent Examiner, Art Unit 1615